REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated October 17, 2006 are respectfully requested.

I. Amendments to the Claims

Claim 8 has also been amended to delete a stray comma at the end of the claim.

II. Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 4, 6, 8, 10, and 11 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement for the use of polypeptides other than those defined by SEQ ID NOs: 2 and 3.

Claims 1, 3, 4, 6, 8, 10, and 11 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description for the use of polypeptides other than those defined by SEQ ID NOs: 2 and 3.

These rejections are respectfully traversed.

A. Analysis: Legal Standard of Enablement

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. A patent may be enabling even though some experimentation is necessary. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217 (Fed. Cir. 1988).

1. Sufficiency of Applicants' Disclosure in view of the art

The instant claims are directed to a method of increasing the IL-10/IL-12 blood ratio in a human subject suffering from multiple sclerosis and to a method of inhibiting progression of multiple sclerosis in a human subject diagnosed with multiple sclerosis, by administering a certain dose of interferon-tau.

Interferon-tau has been studied and written about in the scientific literature for twenty years (see background section of Applicants' specification). Numerous interferon-tau protein sequences are known in the art and reported in GenBank (see paragraph [0036] of Applicants' specification). Thus, a skilled artisan can easily identify interferon-tau proteins.

A skilled artisan can easily test an interferon-tau protein, in vitro or in vivo, to ascertain its activity and/or its effects on multiple sclerosis. The art recognizes in vivo models of multiple sclerosis (e.g., the EAE model), and there are well-described in vitro models to ascertain activity of interferon proteins (see paragraph [0137] of Applicants' specification).

Thus, Applicants fail to see how the present claims pose an undue experimentation problem for a skilled artisan.

2. Consideration of the Wand's Factors

Nor does an assessment of the Wand's factors suggest that a skilled artisan would be unable to practice the present claims. Each of the Wand's factors are analyzed below.

(i) The nature of the invention and (ii) breadth of the claims: The independent claims are to methods of increasing the IL-10/IL-12 blood ratio in a human subject suffering from multiple sclerosis and of inhibiting progression of multiple sclerosis in a human subject diagnosed with multiple sclerosis, by administering a certain dose of interferon-tau.

As noted above, interferon-tau is known in the art, and has been widely studied. These studies have included structure/function studies of the protein (see, for example, Pontzer, C.H. *et al., J. Interferon Res.*, *14*:133-141 (1994); Pontzer, C.H. *et al., Proc. Natl. Acad. Sci.*, USA, 87:5945 (1990)). Thus, the method relies on use of protein well characterized in the art.

(iii) The state of the prior art and (iv) the predictability of the art: The comments above are relevant to this factor. Interferon-tau is known in the art, has been widely studied, and its structure/function is understood.

(v) The amount of direction or guidance presented and (vi) the presence or absence of working examples: The instant application provides a detailed discussion of various interferon-tau proteins (see paragraph [0036]) and of working examples for preparing interferon-tau proteins and for administering the proteins to animals.

(vii) The quantity of experimentation necessary: A skilled artisan can easily identify an interferon-tau protein and test it in vitro for activity and/or test it in vivo to ascertain whether it has the desired ability to modulate IL-10/IL-12 blood ratio. The instant specification provides numerous examples of administering interferon-tau to animals, taking a blood sample, and analyzing the sample for IL-10 and IL-12. Given the ease with which a skilled artisan can do this, and given the large amount of guidance in the specification, a skilled artisan can readily practice the claimed methods.

On balance, analysis of the factors shows that a skilled artisan would be able to practice, i.e., make and use, the invention without undue experimentation. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

B. Analysis: Legal Standard for Written Description

According to the M.P.E.P. § 2163.02, the objective standard for determining compliance with the written description requirement is "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed."

It is the Examiner's position that since the specification does not describe any polypeptides that are less than 100% identical to SEQ ID NOs 2 or 3 or regions or residues of these sequences that can be modified, the specification does not provide adequate written description for the claimed methods.

Applicants direct the Examiner to paragraph 0036 of Applicants' specification, where numerous prior art interferon-tau sequences are identified by GenBank accession numbers. Paragraph 0037 notes that conservative substitutions can be made, as is apparent to a skilled artisan.

Moreover, and as noted above, interferon-tau is well characterized in the scientific literature, including structure/function studies. The law is quite clear that an applicant need not describe what is already known in the art, and thus there is no requirement that every possible interferon-tau protein that could be used to practice the claimed methods be set forth in the specification. Reconsideration of the written description rejection is respectfully requested.

C. Response to Examiner's Comments

In maintaining the enablement and written description rejections, the Examiner makes several assertions, which are addressed individually.

Examiner's Position: The breadth of the claims is excessive because the claims are drawn to administration of any protein that is at least 80% identical to the polypeptide of SEQ ID NO:2, yet the specification does not teach or provide examples of any protein that is less than 100% identical to the polypeptide of SEQ ID NO:2, and provides no evidence showing that a protein with less than 100% homology to SEQ ID NO:2, when administered to a human suffering from multiple sclerosis, would increase IL-10/IL-12 blood ratio and/or inhibit disease progression.

Applicants' Reply: Interferon-tau has been known in the scientific literature for twenty years (see paragraph [0003] of specification). The various protein sequences of interferon-tau are publicly available, for example in PubMed and in GenBank, as

evidenced by the five publications and/or 12 GenBank accession numbers for various interferon-tau proteins noted in paragraph [0036] of the specification. Moreover, interferon-tau as defined in the application is required to exhibit certain functional characteristics (paragraph [0036]). Given that numerous sequences of interferon-tau are known in the art and that the present application requires the interferon-tau to exhibit certain functional characteristics, Applicants submit that this basis for maintaining the rejection is misplaced.

With respect to the statement that there is no evidence showing treatment with a protein with less than 100% homology to SEQ ID NO:2, this is incorrect. In the examples set forth in the application, patients were treated with SEQ ID NO:3 (see paragraph [0139]). SEQ ID NO:3 has less than 100% homology to SEQ ID NO:2.

In response to an alleged lack of evidence showing inhibition of disease progression with a protein less than 100% homologous to SEQ ID NO:2, Applicants direct the Examiner to the application serial no. 10/824,710, now U.S. Patent No. 7,083,782, in which a Declaration was submitted showing clinical evidence that oral administration of interferon-tau inhibits progression of multiple sclerosis. A courtesy copy of the Declaration of Dr. Normal Kachuck is enclosed.

Examiner's Position: The specification lacks guidance or examples that show a person of ordinary skill in the art how to make, and then use, any polypeptide that is less than 100% identical to SEQ ID NO:2 or 3 in a manner that is commensurate in scope with the claims.

Applicants' Reply: The method of preparing the interferon-tau proteins uses conventional, prior art methods, and a specific example using a DNA sequence that encodes for a desired interferon-tau protein is set forth in the Materials and Methods section of the specification on page 35. In this example, Applicants provided the DNA sequences (SEQ ID NOs:1 and 4) for two exemplary proteins. Since the method of preparation is known in the art, and since a specific example is given in the application, a skilled artisan would be able to prepare any interferon-tau protein based on this guidance. Thus, how to make the protein is well described in the specification.

How to use the protein is also clearly and explicitly set forth in the specification, in the working examples and in the Methods of Use section of the application on pages 26-35. Thus, how to use an interferon-tau protein is fully described in the specification.

Examiner's Position: A skilled artisan would not be able to predict which amino acid residues, or regions of polypeptide of SEQ ID NO:2 could be modified by addition, deletion, or substitution, and still result in a polypeptide capable of increasing blood IL-10/IL-12 ratio or inhibiting disease progression in patients suffering from multiple sclerosis.

Applicants' Reply: As noted above, interferon-tau has been known for more than 20 years, and has been extensively studied. Structure – function studies for interferon-tau are reported in the literature (noted above, and a skilled artisan need make no "predictions" regarding possible modifications to interferon-tau proteins since a skilled artisan need only look to the scientific literature. Unless the Examiner can provide evidence that a skilled artisan would be unable to make modifications to interferon-tau, Applicants submit that this position is simply incorrect.

The Examiner's position also overlooks the extensive understanding in the scientific arts regarding conservative amino acid substitutions. The law is quite clear that an applicant need not re-describe in his application that which is known in the art, and therefore, there is no basis for requiring the present applicants to set forth the various modifications that a skilled artisan would understand can be made to, for example, SEQ ID NOs:2 and 3.

Applicants also remind the Examiner that the use of the term "interferon-tau" in the present claims is bounded by the definition set forth in paragraph [0036] requiring that the protein exhibit certain functional characteristics. Moreover, the fact that the present claims are directed to a method of treatment, where the method requires a resultant increase in blood IL-10/IL-12 ratio or an inhibition of disease progression sets a boundary regarding the functionality of the interferon-tau administered.

Accordingly, withdrawal of the rejections based on 35 U.S.C. §112, first paragraph is respectfully requested.

III. Rejections Under 35 U.S.C. § 103

Claims 1, 3, 4, 6, 8, 10, and 11 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Soos et al. (WO 97/033607, "Soos"), in view of Boxel-Dezaire et al. (Ann. Neurol., 45:695-703 (1999), "Boxel-Dezaire"), and further in view of Petereit et al. (*J. Neurol. Sci.*, 206:209-214 (2003), "Petereit"). Reconsideration of the rejection is respectfully requested.

Summaries of the present claims and of the cited art are provided in Applicants' response submitted July 24, 2006.

A. Analysis

In maintaining this rejection, the Examiner alleges that although Soos does not teach oral administration at the presently claimed dose of 5×10^8 Units/day, there is nothing in the disclosure that teaches away from this dosage.

Applicants submit that it is not required that Soos provide a teaching away - this is not the legal standard for obviousness. According to the M.P.E.P. § 2143, "to establish a prima facie case of obviousness, requires, inter alia, that "the prior art references (or references when combined) must teach or suggest all the claim limitations."

Upon application of the correct legal standard, that the cited documents teach or suggest all of the claim limitations, it is seen that Soos does not teach the claimed dosage range. Soos discloses a dose range of between about "1×10^5 and 1×10^8, preferably between about 1×10^6 and 1×10^7 units/day" (page 20, lines 1-2).

Nor does Soos suggest a dose higher than the dosage range disclosed in Soos. There is nothing from a reading of Soos alone or in combination with van Boxel-Dezaire and Petereit, that suggests to a skilled artisan that the dose should be increased beyond the range disclosed in Soos.

In maintaining the obviousness rejection, the Examiner also asserts that there is no correlation between the induced IL-10 levels and the prognosis of the patients.

While applicants do not believe it is necessary to show such a prognosis, especially for claim 1 which is directed only to a method of increase IL-10/IL-12 blood ratios, the Examiner is directed to the Declaration of Norman Kachuck, submitted in a related case noted above.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

IV. Double-Patenting Rejections

A. Claims 1, 3, 4, 6, 8, 10, and 11 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims of copending Application Serial Nos. 10/825,382, 10/825,457, 10/824,710, 11/040,706, and 10/884,741, pending acceptance of a Terminal Disclaimer.

Applicants request the previously-submitted Terminal Disclaimer be accepted.

B. Claims 1, 3, 4, 6, 8, 10, and 11 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 17, and 18 of copending Application Serial No. 11/112,369 ('the '369 application'). This rejection is traversed.

B1. Analysis

Rather than reiterate the comments presented in the response submitted July 24, 2006, Applicants will directly address the Examiner's reasons for maintaining this rejection.

The Examiner asserts that "identifying a multiple sclerosis patient would inherently identify a patient with an IL-10 deficiency, and therefore the '369 application is an obvious variant of the instant application."

The instant claims, compared to the '369 claims, lack a step of "identifying a subject having an IL-10 deficiency." The Examiner's allegation that practicing the present claims, where interferon-tau is administered an a person with multiple sclerosis, inherently identifies a patent with an IL-10 deficiency assumes that all MS patients have

an IL-10 deficiency. There is no evidence in the record on this point, and in fact the cited secondary documents of Petereit and van Boxel-Dezaire would suggest otherwise. Petereit makes clear that IL-10 production in MS patients is low during active disease phases and IL-10 production increase during stable phases of the disease (page 212 of Petereit). Thus, patients with MS at best have a temporal IL-10 deficiency, thus, it cannot be stated or assumed that identification of a person with MS identifies a person with an IL-10 deficiency.

Accordingly, applicants maintain that the claims of the instant application are not a mere invention of the '369 application, since identifying a subject with MS does not inherently identify a patient with an IL-10 deficiency. Accordingly, withdrawal of the obviousness-type double patenting rejection over the '369 application is respectfully requested.

V. Conclusion

In view of the foregoing, the claims pending in the application comply with the requirements of 35 U.S.C. § 112 and patentably define over the applied art. A Notice of Allowance is, therefore, respectfully requested. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 838-4402.

Respectfully submitted,
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Date: 1·17·07

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